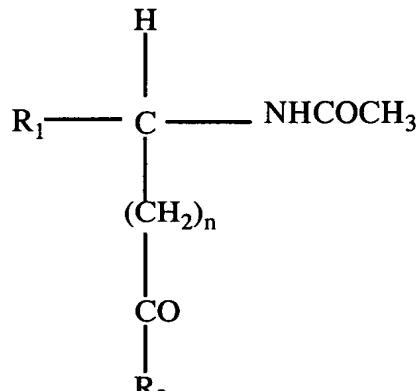


wherein said N-acetyl amino acid is N-acetyl-proline or has the formula:



wherein R<sub>1</sub> is H or an alkyl or aralkyl group having 1 to 14 carbon atoms; n is an integer; R<sub>2</sub> is OH, NH<sub>2</sub> or OR<sub>3</sub>; and R<sub>3</sub> is an alkyl, aralkyl or aryl group having 1 to 9 carbon atoms which may be saturated or unsaturated, straight or branched chain or cyclic form; H attached to a carbon atom may be substituted by I, F, Cl, Br or an alkoxy group having 1 to 9 carbons; and R<sub>1</sub> may carry OH, SH, SCH<sub>3</sub>, COOH, NH<sub>2</sub>, CONH<sub>2</sub>, guanidine or heterocyclic group,

and wherein said N-acetyl amino acid is not N-acetylcysteine or a derivative thereof, and

(C) a cosmetic, pharmaceutical or other topical agent.

#### REMARKS

#### **Introduction**

This communication replies to the Office Action mailed May 26, 1999.

The specification is amended to correct a typographical oversight in the formula describing the N-acetyl amino acids that may be used in accordance with the present invention. In particular, the specification is amended to clarify that R<sub>1</sub> may be NH<sub>2</sub>. It would have been clear to one of skill in the art that the originally filed specification

included N-acetylamino acids having the disclosed formula wherein  $R_1$  is  $NH_2$ . In this vein, Applicants' note that the specification describes N-acetyl-lysine as an exemplary N-acetylamino acid. Specification at page 9, line 16. N-acetyl-lysine is an example of a compound of the disclosed formula for N-acetylamino acids in which  $R_1$  is  $NH_2$ . Additionally, originally filed claims 3, 7, 13 and 17 recite N-acetyl-lysine. These claims depend from claims reciting the formula describing the N-acetylamino acids. Accordingly, no new matter is added.

Additionally, Applicants would like to clarify that the formula for N-acetylamino acids does not accommodate the structure of N-acetyl-proline. In particular, in N-acetyl-proline the carbon atom to which  $R_1$  is attached would be part of a ring structure. In reviewing the application, Applicants noticed this oversight. Applicants note, however, that N-acetyl-proline is described as an exemplary N-acetylamino acid on page 9, lines 17-18, and claimed in several original claims (e.g. claim 3). Accordingly, where appropriate to more accurately define the invention, the claims are drafted to recite N-acetyl-proline in addition to the generic formula describing other N-acetylamino acids according to the present invention. (The amendments to the other claims, which delete the recitation of the formula for N-acetylamino acids in favor of a Markush group recitation of selected N-acetylamino acids, also more accurately define the claimed invention.)

Claims 1, 6-9, 11, and 15 are amended. Claim 1 is amended to delete the recitation of the formula for N-acetylamino acids in favor of a Markush group recitation of selected N-acetylamino acids. Support for the Markush group of selected N-acetyl amino acids is found, for example, on pages 9-10 of the specification and originally filed claim 3. Applicants note that the Markush group of N-acetylamino acids does not include N-acetyl-proline or salts of N-acetyl-glutamic acid. Claim 6-9 are amended to change the dependency to claim 21. Claim 11 also is amended to delete the recitation of the formula for N-acetylamino acids in favor of a Markush group recitation of selected N-acetylamino acids. Support for the Markush group of selected N-acetyl amino acids is found, for example, on pages 9-10 of the specification and originally filed claim 3. Applicants note that the Markush group of N-acetylamino acids does not include salts of N-acetyl-glutamic acid.



Claim 15 is amended to be independent. In addition, the examiner will note that N-acetyl-proline is recited in addition to N-acetylamino acids having the proscribed formula. As explained above, this amendment serves to more clearly recite the claimed invention.

Claims 10 and 20 are amended to correct an inadvertent typographical error. Specifically, a misplaced comma is deleted from in-between the words "clobetasol" and "propionate."

New claims 21-23 are added. Claim 21 incorporates the subject matter of claim 5. New claim 22 recites a composition comprising (A) a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or dermatological disorders and (B) at least 1% by total weight of the composition of at least one compound selected from the group consisting of N-acetyl aldosamines, N-acetylamino acids, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof. New claim 23 recites a composition comprising (A) a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or dermatological disorders, (B) at least 1% by total weight of the composition of at least one compound selected from the group consisting of N-acetyl aldosamines, N-acetylamino acids, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof, and (C) a cosmetic, pharmaceutical or other topical agent. Support for claims 22 and 23 is found throughout the specification and original claims. The recitation of at least 1% by total weight of the composition of at least one compound selected from the group consisting of N-acetyl aldosamines, N-acetylamino acids, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof is supported, for example, on page 17, lines 8-22.

Upon entry of the foregoing amendments, claims 1, 2, 4, 6-12, and 14-23 are presented for examination. Claims 3, 5, and 13 are canceled without prejudice or disclaimer. In view of the foregoing amendments and subsequent remarks, Applicants respectfully request reconsideration of the present application.

**Examiner's Rejections****Rejections Under 35 U.S.C. §§ 102 and 103 Over Friedman *et al.***

In paragraph 2 of the Action, the Examiner rejects claims 1, 3-5, 7-9, 11, 13-15, 17 and 18, under 35 U.S.C. § 102(b), as anticipated by Friedman *et al.* (US Patent No. 5,932,622). In paragraph 5 of the Action, the Examiner also rejects claims 1, 5, 9, 10, 15, 19, and 20, under 35 U.S.C. § 103(a), as unpatentable over Friedman. Applicants respectfully traverse these rejections.

Friedman discloses a water-in-oil emulsion composition that is alleged to be effective in "super-moisturizing" the skin. The disclosed emulsion contains a di-alkali metal salt of N-acetyl glutamic acid. Sodium and potassium salts are disclosed as being preferred. Friedman is limited to di-alkali metal salts of N-acetyl-glutamic acid in water-in-oil emulsions. No other N-acetyl compound is disclosed or suggested in Friedman. In fact, Friedman states that the alleged "super-moisturing effect" is unique to di-alkali metal salts of N-acetyl-glutamic acid formulated in water-in-oil emulsions. See col. 2, lines 55-57 ("It is presently believed that the *unique* ability of these [dialkali metal salts of N-acetyl-glutamic acid] compounds to bind to water is due to their electronic configuration when ionized.") and col. 3, lines 25-27 ("The use of the water-in-oil emulsion is believed *necessary* to obtain a significant moisturizing effect.") (emphasis added).

The claimed invention, as amended, is not anticipated by Friedman. Claims 1, 2, and 4 recite compositions comprising (A) a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or dermatological disorders and (B) a therapeutically effective amount of at least one compound selected from the group consisting of N-acetyl aldosamines, N-acetyl amino acids, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof, wherein the N-acetyl amino acid is selected from a Markush group of selected compounds. (This Markush group does not recite salts of N-acetyl-glutamic acid.) Rather, the claims, with regard to glutamic acid recite N-acetyl-glutamic acid and isomeric or nonisomeric, free acid, lactone, amide, or ester forms thereof. Accordingly, Friedman, which only discloses di-alkali metal salts of N-acetyl-glutamic acid in water-in-oil emulsions, does not anticipate the invention recited in claims 1, 2, and 4.

Moreover, Friedman contains no suggestion of the claimed invention. Friedman teaches the disclosed "super-moisturizing" effect is limited to di-alkali metal salts of N-acetyl-glutamic acid formulated in water-in-oil emulsions. As such, Friedman provides no motivation for one of skill in the art to arrive at the claimed invention. Rather, Friedman teaches away from the use of other N-acetyl compounds in view of the disclosure that the "super moisturizing" effect is limited to di-alkali metal salts of N-acetyl-glutamic acid formulated in water-in-oil emulsions.

In a similar vein, claims 11, 12, and 14 are not anticipated or suggested by Friedman. These claims recite methods for treating cosmetic conditions and dermatological disorders comprising topically applying a composition comprising (A) a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or dermatological disorders and (B) a therapeutically effective amount of a composition comprising at least one compound selected from the group consisting of N-acetyl aldosamines, N-acetyl amino acids and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof, wherein the N-acetyl amino acid is selected from a Markush group of selected compounds. This Markush group does not recite salts of N-acetyl-glutamic acid. Rather, the claims, with regard to glutamic acid, recite N-acetyl-glutamic acid and isomeric or nonisomeric, free acid, lactone, amide, or ester forms thereof. Accordingly, Friedman, which only discloses a method of treating dry skin by applying di-alkali metal salts of N-acetyl-glutamic acid in water-in-oil emulsions, does not anticipate the invention recited in claims 1, 2, and 4.

Likewise, Friedman contains no suggestion of the claimed methods. Again, Friedman provides no motivation for one skill in the art to arrive at the claimed methods for the treatment of various cosmetic conditions and dermatological disorders invention. Rather Friedman teaches the disclosed "super-moisturizing" effect is limited to di-alkali metal salts of N-acetyl-glutamic acid formulated in water-in-oil emulsions, and therefore teaches away from the use of N-acetyl compounds in the claimed methods.

Claims 21, and 6-10 which depend therefrom, recite compositions comprising (A) a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or dermatological disorders, (B) a therapeutically effective amount of at least one compound

selected from the group consisting of N-acetyl aldosamines, N-acetylamino acids, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof, and (C) a cosmetic, pharmaceutical or other topical agent. Claims 15-20 recite methods for treating cosmetic conditions and dermatological disorders comprising topically applying such compositions. These claims are not anticipated or suggested by Friedman.

The compositions recited or topically applied in claims 6-10, 15-20, and 21 comprise a cosmetic, pharmaceutical or other topical agent, in addition to a N-acetyl compound and acceptable vehicle. As the specification discloses, the present inventors have discovered that N-acetyl compounds in combination with a cosmetic, pharmaceutical or other topical agent create an enhanced or synergistic effect. Specification at pages 13-15. Friedman does not disclose or suggest the use of a cosmetic, pharmaceutical or other topical agent in combination with a N-acetyl compound. Hence, Friedman does not disclose or suggest the invention recited in claims 6-10, 15-20, and 21.

For at least the reasons state above, Applicants submit that the invention recited in the pending claims, as amended, is not anticipated or suggested by the disclosure of Friedman. Thus, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §§ 102 and 103 over Friedman.

Rejections Under 35 U.S.C. §§ 102 and 103 Over Kealey *et al.*

In paragraph 2 of the Action, the Examiner rejects claims 1, 3-5, 7-9, 11, 13-15, 17 and 18, under 35 U.S.C. § 102(b), as anticipated by Kealey *et al.* (U.S. Patent No. 5,378,455). In paragraph 5 of the Action, the Examiner also rejects claims 1, 5, 9, 10, 15, 19, and 20, under 35 U.S.C. § 103(a), as unpatentable over Kealey. Applicants respectfully traverse these rejections.

Kealey discloses compositions for topical application to the skin or hair for reducing or retarding hair growth, or for eliminating unwanted hair. These disclosed depilatory compositions are based upon the use of inhibitors of enzymes involved in the conversion of glutamine to pyruvate or lactate and comprise an effective amount of an inhibitor of glutamine metabolism and a cosmetically acceptable vehicle. The disclosed compositions may also comprise hair lightening agents (kojic acid), conventional hair removal agents,

antiperspirants and deodorants, and other cosmetic adjuncts, such as oils, emulsifiers, surfactants, antioxidants, sunscreens, buffers, activity enhancers, colorants, perfumes, and thickeners. Examples 5-7 of Kealey disclose compositions which contains 0.6% w/v of N-acetyl-proline. The use of N-acetyl-proline is not mentioned anywhere else in the specification. Moreover, the specification is totally devoid of any explanation as to the purpose of N-acetyl-proline in the compositions of Examples 5-7 of Kealey.

The claimed invention, as amended, is not anticipated by Kealey. Composition claims 1, 2, 4-10 (as amended) and 21 do not recite N-acetyl-proline as one of the claimed N-acetylamino acids. Accordingly, Kealey cannot anticipate these claims. Composition claims 21 and 23, while encompassing N-acetyl-proline, also recite that the N-acetyl aldosamine, N-acetylamino acid, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof accounts for at least 1% by total weight of the composition. Because Kealey only discloses N-acetyl-proline in 0.6% w/v, Kealey cannot anticipate the claimed compositions

Furthermore, Kealey does not suggest the claimed compositions. As noted above, Kealey only discloses a small quantity of N-acetyl-proline. No other N-acetyl compound is disclosed and there is no suggestion that any N-acetyl compound other than N-acetyl-proline may be used in the disclosed hair removal compositions. Moreover, Kealey provides no reason for the inclusion of N-acetyl-proline in examples 5-7.

Turning to method claims 11, 12, and 14-20, Kealey also is not anticipatory. The claimed methods are for treating cosmetic conditions and dermatological disorders comprising topically applying a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or dermatological disorders, and a therapeutically effective amount of at least one compound selected from the group consisting of N-acetyl aldosamines, N-acetylamino acids, and isomeric or nonisomeric, free acid, salt, lactone, amide, or ester forms thereof. Kealey is directed to methods of removing hair or retarding hair growth, not the treatment of cosmetic conditions or dermatological disorders. Accordingly, Kealey does not disclose the claimed methods. Additionally, Kealey contains no suggestion that the disclosed hair removal compositions could also be used to treat cosmetic conditions or dermatological disorders.

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For at least the reasons state above, Applicants submit that the invention recited in the pending claims, as amended, are not anticipated or suggested by the disclosure of Kealey. Thus, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §§ 102 and 103 over Kealey.

Rejections Under 35 U.S.C. §§ 102 and 103 Over Green *et al.*

In paragraph 3 of the Action, the Examiner rejects claims 1, 2, 4-6, 8, 9, 11, 12, 14-16, 18 and 19, under 35 U.S.C. § 102(b), as anticipated by Green *et al.* (US Patent No. 5,525,336). In paragraph 5 of the Action, the Examiner also rejects claims 1, 5, 9, 10, 15, 19, and 20, under 35 U.S.C. § 103(a), as unpatentable over Green. Applicants respectfully traverse these rejections.

The Examiner characterizes Green as disclosing “a composition for protecting the skin comprising N-acetyl-D-glucosamine in a cosmetically acceptable vehicle ... and optionally protectants such as moisturizers and sunscreens.” Applicants respectfully submit that Green does not contain such a disclosure.

Green does not disclose N-acetyl-glucosamine in a cosmetically acceptable vehicle. Green discloses cosmetic compositions comprising corneocyte proteins and transglutaminase in a cosmetically acceptable vehicle. These compositions may additionally comprise a cellulosic film-former. Green discloses the polysaccharide chitin as an examples of a suitable film-former. Green points out that “the chemical structure of the cellulosic film-former component is distinguished from that of the mucopolysaccharide component in predominantly containing monosaccharide repeating units, N-acetyl-D-glucosamine in the case of chitin.” Col. 7, lines 16-22. Hence, the mention of N-acetyl-D-glucosamine in Green only is in the context of the being the monosaccharide repeating units of chitin. Green does not disclose, or imply, that N-acetyl-D-glucosamine may be used in a cosmetic composition. Thus, Green does not disclose topical compositions comprising N-acetyl-D-glucosamine, and is therefore not properly cited against the claimed invention.

In view of the foregoing, it is apparent that Green does not disclose topical compositions comprising N-acetyl-D-glucosamine. Consequently, Applicants respectfully

request that the rejections, under 35 U.S.C. §§ 102 and 103, in view of Green be reconsidered and withdrawn.

### Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the present claims are in condition for allowance. An early notice in this regard is respectfully requested. Should the Examiner have any questions regarding the present application or believe that further discussion will advance prosecution, the Examiner is invited to contact the undersigned at the number listed below.

Respectfully submitted,

Nov. 24, 1999

Date



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